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Letter to the Editor

A psychotic episode associated with the Atkins Diet in a patient with bipolar disorder

To the Editor:

Studies have suggested that a ketogenic diet is beneficial for epilepsy, both in adults (1) and in children (2). As antiseizure medications have proved to be effective treatment for bipolar disorder, the question has arisen whether the ketogenic diet, or other diets, may be effective in the treatment of bipolar disorder (3). Dietary omega-3 fatty acids have been found to lengthen remissions in bipolar disorder (4). But in one study that examined the effect of the ketogenic diet on bipolar disorder in valproate-resistant patients, no effect was found (5). We describe the case of a patient with bipolar disorder maintained on valproic acid, who developed mania shortly after initiating the Atkins diet.

The patient is a 54-year-old veteran who first developed bipolar disorder in the mid-1990s. His most recent psychiatric admission was in October 2001. Discharge psychiatric medications were divalproex, 1.5 g total per day, clonazepam, 1 mg at HS, and quetiapine, total daily dose 700 mg. From October 2001 until June 2003, the patient had no psychiatric complaints recorded by his caseworker with the exception of mild anxiety. On June 12, 2003, the patient told his caseworker that he started the Atkins diet. On June 25, the patient reported that he was not sleeping well, and clonazepam was increased to 1.5 mg. On July 10, because of continued insomnia, his divalproex was increased to 2 g/day. On July 22, the patient's family voiced concerns over his increasingly bizarre behavior and paranoia. On July 24, the patient had multiple somatic complaints, and on July 30, he complained of multiple odors and was hyperverbal. A total of 25 mg of diazepam/day was added to his medication regimen. On August 8, the caseworker noted that money was missing from the patient's bank account. The patient continued to refuse hospital admission until August 12, when he was evicted after covering the entire apartment in talcum powder, and flooding the apartment with water from his bathtub, resulting in the collapse of the ceiling of the apartment downstairs. The time course of the patient's diet and symptoms is outlined in Fig. 1.

At presentation to the hospital, the patient's weight was recorded as 189 pounds. Mood was irritable and expansive. Thought process was rambling and tangential. Thought content included somatic preoccupation and delusions with religious references. He was not oriented to day or date.

He was placed on a regular diet, and treated with a continuation of his preadmission medications. His weight increased rapidly, his mood stabilized, and his delusions gradually improved until his discharge on September 8, 2003.

One possible connection between diet and the development of mania in this patient is a relationship between ketosis and valproate metabolism.

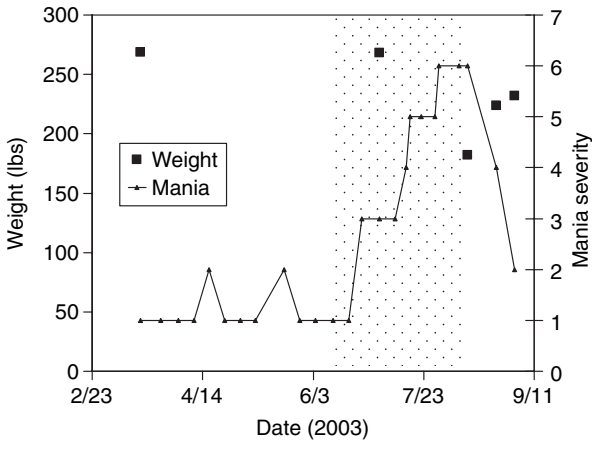

Fig. 1. Patient weight and severity of manic symptoms prior to admission. Symptoms were recorded from notes made by the patient's caseworker. Shaded area represents the period of the patient's diet. Symptom severity was divided on a 6-point scale: 1 = stable mood; 2 = some complaints of anxiety; 3 = insomnia; 4 = bizarre behavior with intact reality testing; 5 = disorientation, primarily to date; and 6 = severe psychosis.

Valproate, or 2-propylpentanoic acid, is a branched-chain fatty acid that is metabolized both by glucuronization and oxidation. There is significant variation in the pattern of valproate metabolism within and between individuals (6). The oxidative pathway occurs within the mitochondria and is subject to auto-induction (7) and is capable of complete metabolism of valproate via beta oxidation to carbon dioxide and ketone bodies (8). During low-carbohydrate diets or starvation, gluconeogenesis is stimulated through multiple mechanisms, including increased mitochondrial transport of fatty acids, resulting in the formation of ketones. It is conceivable that the stimulation of fatty acid transport and metabolism by dietary changes could lower plasma levels of valproate.

An alternative explanation in the present case is that metabolic conditions related to the diet contributed directly to the development of mania, independently of changes in the plasma level of valproate. Mania has been precipitated in Muslim bipolar patients by changes in 'social rhythm' during Ramadan, a month in which fasting is observed (9). Elevation of mood has been reported in obese patients during low-calorie, limited-carbohydrate diets, whether or not ketosis develops (10). Mood changes during fasting may be related to changes in neuroendocrine function (11).

In summary, the close temporal relationship between the initiation of the Atkins diet by this patient and the subsequent development of mania suggests a relationship between diet and bipolar disorder. Further studies are necessary to elucidate this relationship, as well as to investigate the effects of dietary changes on the metabolism of valproic acid.

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